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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/654,281	09/01/2000	John M. Sedivy Ph.D.	3564/1010	5838

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EXAMINER	
YU, MISOOK	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 10/17/2002

18

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/654,281	SEDIVY PH.D. ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *1-32, and 38-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election of group VII, claims 33-37 in Paper No. 17 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-32, and 38-45 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 11.

Claims 1-45 are pending and claims 33-37 are examined on merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 33-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 33 recites the limitation "the activity" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 33 recites "the activity of an RKIP-sensitive kinase" but it is not clear what the metes and bounds are for the phrase. Neither the specification nor the claims define the phrase. Since the specification mostly discusses about kinase activity of proteins in MEK/MAPK pathway, this examiner will assume that the phrase means kinase activity of the proteins in said pathway. However this treatment does not relieve applicant the burden of responding this rejection.

Claim 33 recites "an RKIP-sensitive kinase" but it is not clear what the metes and bounds are for the phrase. The 3rd paragraph at page 13 does not define what is "an RKIP-sensitive kinase".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 33-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had **possession** of the claimed invention. The claim is drawn to a method of inhibiting ***a genus of kinases*** called "RKIP-sensitive kinase" using ***a genus of agents***.

The specification teaches that:

1) Full-length RKIP (Raf kinase inhibitor protein) also known as phosphatidylethanolamine-bindidng protein in the art binds to the full-length Raf-1 at page 77, line 3.
2) Several proteins from many different species have the RKIP motif of human RKIP at Fig. 1.
3) The human RKIP protein inhibits Raf-1 kinase activity and disrupts interaction of Raf-1 kinase and MEK at Fig. 8 and Example 5 at page 82 and 83, but the does not inhibit any other kinase tested in Fig. 5 (see also page 83, 1st paragraph).

Based on a species of so-called "**RKIP-sensitive kinase**", i.e., Raf-1, and based on a species of **agents**, i.e., the human RKIP, one cannot predict additional species of "RKIP-sensitive kinase" and additional species of agents other than the one shown in the instant specification. Since the genus include a large number of unpredictable species, possession of a species from each of the two genuses is not seen as sufficient to reasonably convey possession of the entire genus. It is concluded that applicant adequately describe the method to inhibit activity of human Raf-1 kinase using the human RKIP protein shown in Fig. 8.

Claims 33, 34, 36, and 37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to **enable** one skilled in the art to which it pertains, or with which it is most nearly connected, to **use** the invention. The claim is drawn to a method of inhibiting RKIP-sensitive kinase using agents. The specification teaches that the full-length RKIP inhibits Raf-1 kinase (see the specification summary above under Written Description rejection), but the specification does not teach any other agent that inhibits an RKIP-sensitive kinases. The specification provides insufficient guidance with regard to what kinds of "agents" able to inhibit an activity of an RKIP-sensitive kinase and provides no working examples which would provide guidance to one skilled in the art. Therefore, it appears that undue experimentation would be required to practice the claimed inventions.

Claim 35 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to **enable** one skilled in the art to which it pertains, or with which it is most nearly connected, to **use** the invention. The claim is drawn to a method of inhibiting "RKIP-sensitive kinase" comprising contacting said kinase with a polypeptide comprising an RKIP motif. Since the specification says at pages 66-76, especially at 72-74 that the use for instant invention is to modulate cell proliferation and apoptosis, the claim is interpreted as drawn to method of regulating cell proliferation or apoptosis, comprising the active step of contacting cell expressing RKIP-sensitive kinase with a polypeptide comprising RKIP motif. The specification at the paragraph bridging page 73 and 74 says that cell lines resistant to apoptosis were rendered sensitive to apoptotic stimuli by the expression of RKIP. However, the specification does not teach how to regulate apoptosis or proliferation of cell by contacting the RKIP. A peptide or protein must accomplish several tasks to be effective *in vivo*. It must be delivered into the target cells and interact at the proper site of action. The specification does not teach how how to target the RKIP protein to cytosol of a cell. Berg et al (05 March 1999, Cancer Research 59, 1180-1183) teach at the abstract, 1st paragraph column 1 and 5th paragraph column 2 of

page 1181 that targeting macromolecules to cytosol is not an easy task. Also protein and peptide concentration must be at a sufficient concentration and for a sufficient period of time. In addition, variables such as biological stability, half-life are important parameters to be considered for inducing or regulating apoptosis with a protein. The proteins may be inactivated inside cell before producing a sufficient effect, for example, by degradation, immunological activation or due to an inherently short half life of the formulation. Peptide or polypeptide degradation is a problem well known in the art, in view of the presence of different proteases present inside cell, and at the surface of cells. US PAT 4,925,677 teaches that a protein, albumin is degradable by proteolytic enzymes (column 4 lines 4-18). Kastin, AJ, 2001, Life Science, 69(11): 1305-12, teach at the abstract and paragraph bridging page 1310 and 1311 that peptides are degraded at different regions in rat cerebral microvessels. Frost, SJ, 1993, J Cell Biochem, 52(2): 227-36 teach that peptides are degraded by cell-surface peptidase activity on endothelial cells (see the abstract). Selbo et al (2002, Tumour Biol 23, 103-12, abstract only) teach that a major intracellular barrier to the application of therapeutically interesting proteins is degradation of macromolecules

Thus, based on the apoptosis data by the RKIP expressed inside cell by transfected DNA, it could not be predicted that the proteins of the instantly claimed invention could induce apoptosis in cells. The specification provides insufficient guidance with regard to theses issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict the efficacy of the claimed regulating proliferation or apoptosis of cells with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed inventions.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 33, 34, 36, and 37 are rejected under 35 U.S.C. 102 (**b**) as being anticipated by Jelinek et al (March 1996, Molecular and Cellular Biology, vol. 16, pages 1027-1034).

The claims are drawn to a method of inhibiting the activity of RKIP-sensitive kinase, comprising contacting said kinase with an agent, wherein the agent is a polypeptide in claim 34, wherein the kinase is a MAPK/ERK kinase in claim 36, wherein the agent binds to Raf-1 in claim 37. Jelinek et al teach at Figs. 1-5, especially Fig. 3, a method of inhibiting Raf-1 by PTP-1B. Note also the abstract and Materials and Methods section.

Claims 33, and 36 are rejected under 35 U.S.C. 102 (**e**) as being anticipated by US Pat. 6,187,799 (issued Feb. 13, 2001, filed May 22, 1998).

The claims are drawn to a method of inhibiting the activity of RKIP-sensitive kinase, comprising contacting said kinase with an agent, wherein the kinase is a MAPK/ERK kinase in claim 36. US Pat. 6,187,799 in claims 1-7 (columns 31-43) teaches a method of inhibiting raf kinase with several different agents.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 703-308-2454. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-

305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Misook Yu
October 13, 2002

MARY E. MOSHER
PRIMARY EXAMINER
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1600